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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,645	03/19/2004	Giovanni Paternostro	GP-00102.P.1.1	7761
24232	7590	01/25/2005	EXAMINER	
DAVID R PRESTON & ASSOCIATES 12625 HIGH BLUFF DRIVE SUITE 205 SAN DIEGO, CA 92130			HAMA, JOANNE	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 01/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/804,645

Applicant(s)

PATERNOSTRO, GIOVANNI

Examiner

Joanne Hama, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 3/19/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/10/04</u> . | 6) <input type="checkbox"/> Other: ____. |

This Application, filed March 19, 2004, claims benefit to U.S. Provisional Application, 60/456,846, filed March 21, 2003.

Claims 1-24 are pending.

Election/Restrictions

Applicant's election with traverse of Group II (claims 17-24) in the reply filed on December 10, 2004 is acknowledged. The traversal is on the ground(s) that the methods of screening for a gene and methods of screening for an agent are capable of use together. The Examiner has considered the Applicant's arguments and has withdrawn the restriction requirement.

Claims 1-24 are under consideration in this First Office Action.

Information Disclosure Statement

The information disclosure statement filed December 10, 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Copies of all documents have been received except for document D19, Lin, et al. 1998, Extended life-span and stress resistance in the *Drosophila* mutant methuselah. Science, 282:1837-1840.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other

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information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-10, 12-22, 24 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 3-5, 8-19, 21-24, 31 of copending Application No. 10/077,670, published as 2002/0161302, October 31, 2002. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 1-10, 12-16 of the instant application are to a method of screening for a gene affecting cardiac function after or during hypoxia or anoxia. Claim 1 is to a method of screening for a gene affecting cardiac function after or during hypoxia or anoxia, comprising the steps of exposing an adult *Drosophila* to conditions able to induce cardiac hypoxia or anoxia; imaging the heart of said *Drosophila*; measuring the movements of the heart in the image; analyzing the measurements of said movements;

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and identifying a gene affecting the cardiac function of said *Drosophila*. This claim is the similar to claim 1 of '670. Claims 2-5 of the instant application further limit claim 1 and are to: exposing the *Drosophila* to change in temperature (claim 2), said gene affects an age-related change in cardiac function (claim 3), the *Drosophila* is *Drosophila melanogaster* (claim 4), and that imaging of the heart comprises positioning the *Drosophila* under a microscope so that the light beam of the microscope is perpendicular to the frontal plane of the *Drosophila* and is directed onto the heart of the *Drosophila* (claim 5). These claims are similar to claims 2, 3, 4, 8 of '670. Claims 6 and 7 of the instant application depend on claim 5 and are to one contrast enhancement means is combined with said microscope to improve said image of said heart (claim 6) and to a microscope wherein the microscope is a fluorescence microscope, and wherein the *Drosophila* expresses a fluorescent protein (claim 7). These claims are the same as claims 9 and 10 of '670. Claim 8 of the instant application depends on claim 7 and is to a fluorescent protein which is fluorescent green protein. This claim is the similar to claim 11 of '670. Claims 9, 10, 12 of the instant application further limit claim 1 and are to movements of the walls of the heart (claim 9), to analyzing measurements correspond to heart rate (claim 10), and to comparing measurements to a control set of data (claim 12). These claims are similar to claims 12, 13, 14 of '670. Claim 13 of the instant application further limits claim 1 and is to a gene that has a mutation. This is similar to claim 15 of '670. Claims 14 and 16 further limit claim 13 by stating that the mutation causes a change in expression of the gene (claim 14) and that the mutation causes an age-related change in cardiac function (claim 16). These claims are similar

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to claims 16 and 18 of '670. Claim 15 further limits claim 14, wherein the change in expression causes an age-related change in cardiac function and is similar to claim 17 of '670.

Claims 17-22, 24 of the instant application are to a method of screening for agents affecting cardiac function after or during hypoxia or anoxia. Claim 17 of the instant application is to a method of screening for agents affecting cardiac function after or during hypoxia or anoxia, comprising the steps of exposing an adult *Drosophila* to conditions able to induce cardiac hypoxia or anoxia; exposing said *Drosophila* to an agent; imaging the heart of said *Drosophila*; measuring the movements of the heart in the image; analyzing the measurements of said movements; and identifying an effect of said agent on the cardiac function of said *Drosophila* by comparing said analysis to a control. This is similar to claim 19 of '670. Claims 18-22, 24 of the instant application further limit claim 17 and are to exposing the *Drosophila* to a change in temperature (claim 18), to an effect of said agent on age-related changes in the cardiac function is determined (claim 19), to measurements, which are compared to a control set of data (claim 20), to movements, which are movements of the walls of the heart (claim 21), to analysis, which comprises determining the heart rate of the *Drosophila* (claim 22), and to a *Drosophila* that is *Drosophila melanogaster* (claim 24). These claims are similar to claims 19, 21-24, 31 of '670.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Paternostro et al. (2001, Circ. Res. 88:1053-1058, see IDS).

Paternostro et al. teach a method wherein *Drosophila melanogaster* were used to determine the effects of certain agents on cardiac function after or during hypoxia or anoxia. Paternostro et al. teach that Oregon-R flies and transgenic flies that expressed green fluorescence protein (GFP) under the control of an actin promoter were used in their study (page 1054, first column, under heading "Animals"). Paternostro et al. teach that flies were mounted on glass slides and observed with a Nikon Diaphot-TMD inverted microscope. Flies were positioned on their backs, exactly perpendicular to the light path, and fixed in this position by mounting the wings on the glass slide with double-stick tape. Images of the first cardiac ventricle were recorded by using a videocamera and the heart rate was measured from slow-motion replays. End-diastolic and end-systolic dimensions were measured on still images at the midpoint between the 2 major transversal tracheal tubes passing over the first cardiac ventricle (page 1054, first column, under "Measurements of Heart Rates"). Paternostro et al. teach that two protocols were used to stimulate elevations in heart rate as a result of increased ambient temperature (page 1054, first column, fifth paragraph, under "Temperature Stress Test"). Paternostro et al. teach a semiautomated digital image-processing

method to measure heart rate and its variation directly from video signals recorded in a single fly. Video image sequences were stored in the memory of a microcomputer with use of a high-resolution video frame grabber, at a sampling frequency of 30 frames per second. For each fly, a 2-second video sequence (60 frames each), 10 times consecutively, was acquired. Custom software constructed a time-space image signal representing the time course of image intensity along a line segment of pixels that crosses the ventricular lumen transverse to the heart axis (page 1054, second column, under "Automated Heart Rate Detection").

Paternostro et al. teach two agents which have an effect on the heart: anesthesia (page 1055, first column, first paragraph) and temperature (page 1055, first column, third paragraph to page 1056, first column, first paragraph). Paternostro et al. teach that one fly anesthetic, CO₂, was shown to cause cardiac arrest within a few seconds, with resumption of heart beat 20 to 30 seconds after cessation of gas exposure (page 1055, first column, first paragraph, lines 1-5). Another anesthetic, ethyl ether, was shown to depress heart rate in flies. The heart rate was about 12 bpm immediately after ether anesthesia, but increased to about 248 bpm in the same flies after 30 to 40 minutes (page 1055, first column, first paragraph, lines 5-9). In contrast, triethylamine did not cause significant changes in heart rate under the same conditions (page 1055, first column, first paragraph, lines 10-14).

Paternostero et al. also teach that temperature affected heart rate. In the first protocol, Paternostero et al. demonstrated a pronounced effect of age on average heart

rate when the temperature of the flies was raised from 22°C to 28°C. Paternostero et al. teach that the average heart rate measured in 10 day old flies was about 339 bpm, while 31 day old flies was about 301 bpm, and 54 day old flies were about 254 bpm (page 1055, first column, third paragraph to second column, first paragraph).

Paternostero et al. also teach that when flies were at 35°C, there was a decline in heart rate, with increasing age; 10 day old flies had about 440 bpm, 30 day old flies had a rate of about 372, 54 day old flies had a rate of about 288 (page 1055, second column, second paragraph to page 1056, first column, first paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paternostero et al. (2001, Circ. Res. 88:1053-1058, see IDS) or Paternostero U.S. Patent Application No. 10/077,670, published as 2002/0161302, October 31, 2002, in view of St. Johnston (2002, Nat. Rev. Genet., 3:176-88) .

Paternostro et al. teach a method wherein *Drosophila melanogaster* were used to determine the effects of certain agents on cardiac function after or during hypoxia or anoxia. Paternostro et al. teach that Oregon-R flies and transgenic flies that expressed

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green fluorescence protein (GFP) under the control of an actin promoter were used in their study (page 1054, first column, under heading "Animals"). Paternostero et al. teach that flies were mounted on glass slides and observed with a Nikon Diaphot-TMD inverted microscope. Flies were positioned on their backs, exactly perpendicular to the light path, and fixed in this position by mounting the wings on the glass slide with double-stick tape. Images of the first cardiac ventricle were recorded by using a videocamera and the heart rate was measured from slow-motion replays. End-diastolic and end-systolic dimensions were measured on still images at the midpoint between the 2 major transversal tracheal tubes passing over the first cardiac ventricle (page 1054, first column, under "Measurements of Heart Rates"). Paternostero et al. teach that two protocols were used to stimulate elevations in heart rate as a result of increased ambient temperature (page 1054, first column, fifth paragraph, under "Temperature Stress Test"). Paternostero et al. teach a semiautomated digital image-processing method to measure heart rate and its variation directly from video signals recorded in a single fly. Video image sequences were stored in the memory of a microcomputer with use of a high-resolution video frame grabber, at a sampling frequency of 30 frames per second. For each fly, a 2-second video sequence (60 frames each), 10 times consecutively, was acquired. Custom software constructed a time-space image signal representing the time course of image intensity along a line segment of pixels that crosses the ventricular lumen transverse to the heart axis (page 1054, second column, under "Automated Heart Rate Detection"). In U.S. Patent Application No. 10/077,670,

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published as 2002/0161302, October 31, 2002, Paternostero teach that contrast enhancement can be combined with a microscope to improve the image of the heart.

While Paternostero et al. teach the effects of temperature and anesthesia on heart rate in flies, they do not teach the effects of genes on heart rate in flies.

St. Johnston teaches methods of generating mutations in *Drosophila*. The first method taught by St. Johnston is through the use of ethyl methane sulphonate (EMS). According to St. Johnston, EMS is the most commonly used mutagen in *Drosophila* because it is easy to administer and causes the highest frequency of mutations. It mainly induces single-base changes (point mutations), which disrupt gene function by causing missense or nonsense mutations. Using the standard mutagenesis protocol with 25mM EMS, the mutation rate for the average gene is about 1 in 1000. The second method taught by St. Johnston is P-transposable elements. In this method, a mutated gene is rapidly and easily identified using the P-element as a tag. P-elements, however, are very inefficient mutagens, so the most common approach is to screen the large collection of P-element insertions that are available from the Berkley *Drosophila* Genome Project, rather than generating new insertions by mobilizing the P-element oneself. The existing collection contains insertions in about one-quarter of the essential genes. Most genes are predicted to be cold spots for P-element insertions, so saturation screens cannot be carried out (page 177, Box 1, "Mutagenesis in *Drosophila*").

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Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the P-element mutated flies generated by the Berkeley Genome Project or to generate flies with point mutations in the genome, via the methods described by St. Johnston in the method described by Paternostro et al. to identify flies with a change in cardiac function.

One having ordinary skill in the art would have been motivated to use the mutant flies generated by the Berkeley Genome Project or generate mutant flies by EMS, in order to obtain a set of flies suitable for use in a screen detecting changes in heart function.

There would have been a reasonable expectation of success given the results of Paternostro et al., who taught a method of detecting changes in cardiac function in flies treated with anesthesia and in flies introduced to different ambient temperatures.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

Joe Winters
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